

## **Program Announcements (PA'S)**

### **STUDIES ON OBESITY**

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National Institute of Diabetes and Digestive and Kidney Diseases

National Heart, Lung, and Blood Institute

National Institute of Child Health and Human Development

National Cancer Institute

National Institute on Aging

National Center for Nursing Research

National Institute of Neurological Disorders and Stroke

National Institute of Arthritis and Musculoskeletal and Skin Diseases

National Institute on Deafness and Other Communication Disorders

National Institute of Mental Health

## **BACKGROUND INFORMATION**

Research on the biomedical and behavioral aspects of obesity is an important component of the NIH nutrition research program. Obesity is widely prevalent in the United States, affecting both children and adults. Data on body mass index from the second National Health and Nutrition Examination Survey (1976-80) indicated that 24 percent of men and 27 percent of women were overweight (body mass index equal to or greater than 27.8 for men and 27.3 for women). The prevalence of obesity in adults has not declined in the past three decades; some data suggest that its prevalence in children has increased over this time. Obesity is particularly prevalent in minority populations, especially among minority women. Obesity is multifactorial in origin, reflecting inherited, environmental, cultural, and socioeconomic conditions.

Obesity is associated with elevated serum cholesterol levels, elevated blood pressure, and noninsulin-dependent diabetes, and is an independent risk factor for coronary heart disease. It also increases the risk for gallbladder disease and some types of cancer and has been implicated in the development of osteoarthritis of the weight-bearing joints. Obesity acquired during childhood or adolescence often persists into adulthood and increases the risk for some chronic diseases later in life.

The great prevalence of obesity and its physical and mental health consequences make its prevention and treatment a public health priority.

## HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention goals of "Healthy People 2000", a PHS-led national activity for setting priorities. This program announcement is related to the priority areas of nutrition, physical activity and fitness, heart disease and stroke, cancer, diabetes, and chronic disabling conditions. Potential applicants may obtain free of charge a copy of "Healthy People 2000" (Full Report: No. 017-001-474-0, or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (Telephone: 202-783-3238).

## RESEARCH GOALS AND SCOPE

The emphasis of this program announcement is the support of research on the biomedical and behavioral aspects of exogenous obesity. The goals of this research, which includes basic, clinical, and population research, are to establish a clear understanding of the etiology, prevention, and treatment of this multifaceted condition. For example, the determinants of obesity during the early stages of the life cycle need to be identified in order to prevent the onset of obesity early in life and to identify individuals at high risk of becoming obese later in life. Preventive therapies, as well as successful treatment regimens, need to be designed. In order to accomplish these goals, further research is needed on the behavioral and developmental aspects of obesity in terms of its natural history and determinants in infancy, childhood, and adolescence; on the molecular, metabolic, genetic, and neurological aspects of obesity; on the successful treatment of obesity; and on the effects of obesity on health and longevity. A major question with respect to the health implications of obesity is determining the relative roles of body composition, body fat, and the regional distribution of body fat in the morbidity and mortality attributed to obesity. There is also the need to learn more about adipose tissue morphology as a determinant of the pattern of fat distribution and the impaired health and shortened life span associated with the obese state. Finally, more information is needed to support health-based standards of desirable weight for various age, sex, and ethnic groups.

Examples of research areas in obesity of particular interest include, but are not limited to, the following:

### Molecular, Metabolic, and Genetic Factors

- o Mechanisms by which obesity contributes to the development of diseases such as diabetes, coronary heart disease, hypertension, and cancer, as well as possible differences in such mechanisms among different ethnic groups.

- o The contribution of genetic and metabolic factors to obesity, including the molecular and genetic basis of energy metabolism and the nature of genetic aberrations in human obesity.
- o Interactions of genetic and environmental factors, as well as dietary, behavioral, and social factors, in the etiology of obesity and their effects on the ability to lose weight successfully.
- o The contribution of muscle metabolism to energy balance.
- o Methods for measuring body fat distribution and determining its effects on disease.
- o Hypometabolism and factors that influence energy expenditure.
- o Influence of gestational diabetes on subsequent weight gain of offspring.
- o Role of nutrient composition of the diet in energy balance.

#### Neurological and Endocrine Factors

- o The neurophysiology of ingestive behavior, including an understanding of the mechanisms of anorexia.
  - o Central nervous system/hypothalamic/autonomic nervous system (including sympathetic nervous system) control of energy intake and expenditure, including the neuroanatomical organizations and pathways that control food intake and the behavioral, hormonal, and metabolic mechanisms by which such pathways influence satiety mechanisms and body weight.
  - o Role of the brain in mediating acquisition, extinction, and aversion of associations to gustatory, olfactory, and trigeminal stimulation.
  - o Neuroanatomical pathways connecting the gastrointestinal system to the hypothalamus, and the effect of changes in the gastrointestinal system on the electrophysical activity in the hypothalamus.
  - o Functional and structural alterations in the brain resulting from changes in food intake in animals, as well as gustatory, olfactory, and trigeminal stimulation.
  - o Neurological mechanisms of taste, smell, and common chemical reception in a variety of animal models.
- #### Behavioral and Developmental Factors
- o Behavioral interventions to prevent and treat obesity at all ages and in various population groups, including minority populations.

- o Behavioral change strategies for weight loss and to prevent relapse after weight loss.
- o Application of the techniques of behavioral neuroscience to the prevention and treatment of obesity.
- o Mechanism of action of reinforcers of food intake and physical activity.
- o Sensory-specific studies of habituation phenomena.
- o Genetic/environmental/behavioral interactions.

### Treatment of Obesity

Due to the serious health implications of obesity, research must continue to find successful measures to treat obesity and to prevent its recurrence. Various treatments that need to be examined include the use of hypocaloric regimens, the effects of exercise alone or in combination with caloric restriction on metabolism and subsequent weight loss, and behavioral therapies. Such treatments need to be examined across the various stages of the life cycle and in different risk groups. Treatment outcomes, including regression of risk factors and effects on other medical disorders, need to be examined, including:

- o Treatment models and efficacy in various age groups and in minority populations.
- o Influence of duration of obesity on adverse health effects and response to intervention.
- o Effects of weight cycling on cardiovascular risk factors, fat patterning, and other physiological measures.
- o The effect of mild exercise on appetite and the role of exercise in weight control.
- o Mechanism of action and efficacy of pharmacologic agents in energy balance and weight control.

### Prevention of Obesity

- o Research emphasis on preventing obesity in children, adolescents, and adults and encouraging healthy active lifestyle at all ages.
- o Interventions to reduce sedentary behavior.

- o Evaluation of prevention strategies targeted at specific racial, ethnic, and socioeconomic high-risk groups.

## SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

National Institutes of Health (NIH) policy is that applicants for NIH clinical research grants will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study. Special emphasis should be placed on the need for inclusion of minorities in studies of diseases that disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear and compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial or ethnic group, together with a rationale for its choice. In addition, gender and racial or ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included on grant application form PHS 398 in Sections 2A-D of the Research Plan AND summarized in Section 2E (Human Subjects).

Applicants are urged to carefully assess the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial or ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies or etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is

important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, applicants must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will specifically address whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning a priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants that do not comply with these policies.

## MECHANISM OF SUPPORT

The mechanism of support for this program will be the grant-in-aid (RO1 and R29). The regulations (Code of Federal Regulations, Title 42, Part 52 and Title 45, Part 74) and policies that govern the research grant programs of the Public Health Service will prevail. The award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriated funds for this purpose.

The NIH requires applicants for grants to give added attention (where feasible and appropriate) to the inclusion of minority groups and/or women in the study populations for research. For proposed population-based studies that do not include women and/or minorities, a clear rationale for not including either or both must be provided.

## METHOD AND CRITERIA OF REVIEW

Assignment of Application: Applications will be received by the Division of Research Grants (DRG), NIH, referred to an appropriate study section for scientific review, and assigned to individual Institutes for funding consideration. These decisions will be governed by customary programmatic considerations as specified in the DRG Referral Guidelines.

Review Procedures: Applications in response to this announcement will be reviewed in competition with other applications received in the same review cycle, and in accord with the customary NIH peer review procedures. The initial review for scientific and technical merit will be by a review group composed mostly of non-Federal scientific consultants (study section). Following study section review, the application will be evaluated by the appropriate Institute Advisory Council or Board with respect to the adequacy of the technical merit review and the program relevance of the research proposed. The review criteria customarily employed by the NIH PHS for research grant applications will prevail.

Deadlines: Applications will be accepted in accordance with the usual receipt dates for new applications: October 1, February 1, and June 1.

## METHOD OF APPLYING

Applications should be submitted on form PHS 398 (rev. 10/88) that is available in the business or grants and contracts office at most academic and research institutions and from the Office of Grants Inquiries, Division of Research Grants, NIH, Westwood Building, Room 449, Bethesda, MD 20892, telephone (301) 496-7441. In line 2 on the face page of the application, the phrase, "Studies on Obesity" must be inserted.

For further information, investigators are encouraged to contact one or more of the following individuals:

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This program announcement replaces a previous one published in the NIH Guide for Grants and Contracts, Vol. 13, No. 4, March 30, 1984.

#### AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.848, 93.847, 93.837, 93.865, 93.393, 93.866, 93.854, 93.173, and 93.242. Awards are made under the authorization of the Public Health Service Act, Section 301 (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.